

955,898



PATENT SPECIFICATION

NO DRAWINGS

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No. 6552/62.

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International Classification:—C 07 c

COMPLETE SPECIFICATION

Process for the Production of Carbamic Acid Fluorides or Isocyanates Substituted by Fluorine on Aliphatic Carbon Atoms

- We, FARBENFABRIKEN BAYER AKTIEN-GESELLSCHAFT, of Leverkusen-Bayerwerk, Germany, a body corporate organised under the laws of Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—
- 5 This invention relates to a process for the production of carbamic acid fluorides or isocyanates substituted by fluorine on aliphatic carbon atoms.
- 10 It has been found that in isocyanates which have chlorine substituents on aliphatic carbon atoms, the chlorine atoms can be simply replaced by fluorine by reaction with anhydrous hydrofluoric acid.
- 15 Isocyanates which contain aliphatically combined fluorine atoms are known *per se* and they are prepared by the conventional processes from the corresponding amines by phosgenation or from the carboxylic acids by a Curtius degradation (Ann. 562, 75 (1949); J. chem. Soc. 1956, 3428).
- 20 According to prior knowledge concerning the exchange of chlorine for fluorine in anhydrous hydrofluoric acid, it was not to be anticipated that chlorinated isocyanates can be transformed by the process of the invention into fluorinated isocyanates. Thus, it is known that most nuclear substituents interfere with the exchange of chlorine in benzotrichloride (Ang. Chem. 52,458 (1939)).
- 25 Apart from chlorine, only the phthalimide grouping permits a sufficient fluorination. By way of example, trichloromethyl benzonitrile cannot be further fluorinated with hydrofluoric acid.
- 30 It must be all the more surprising that with the present process, under extraordinarily gentle conditions, the chlorine exchange takes place still more smoothly than with the unsubstituted benzotrichloride. In the latter case, in order to obtain acceptable reaction times, there are always required temperatures which are far above the boiling point of the hydrofluoric acid and necessitate working under pressure (German Patent 670,130). With reaction temperatures of 0° C., several days are necessary and the hydrofluoric acid must be incorporated by condensation in gaseous form in order to avoid secondary reactions.
- 35 It is also known that exclusively resinous products are formed by the action of hydrofluoric acid on benzal chloride. On the other hand, the present invention shows that benzal chloride isocyanates can be fluorinated with hydrofluoric acid.
- 40 Fluorination in the aliphatic series, with the exception of methyl chloroform, cannot be conducted without catalysts, and the latter only at temperatures of 150° C. (Ang. Chem. 52,459 (1939)).
- 45 However, it was also not to be readily expected that the isocyanate group which is very reactive in the aromatic series does not initiate any, or only slight, secondary reactions under the conditions of the present process. Anhydrous hydrofluoric acid is a known Friedel-Crafts-catalyst and it is known that the isocyanate group condenses under the action thereof to acid amides.
- 50 It is certainly stated in German Specification 1,092,462 that aromatic isocyanates can be alkylated in anhydrous hydrofluoric acid, but it could be justifiably assumed that a special case is involved here. From the chemistry concerning anhydrous hydrofluoric acid, it is known that it is just under alkylation conditions that some compounds behave quite differently than otherwise in hydrofluoric acid (Ang. Chem. 56,341 (1943)). For
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- [Price 4s. 6d.]

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International Classification: —C 07 c

COMPLETE SPECIFICATION

**Process for the Production of Carbamic Acid Fluorides or
Isocyanates Substituted by Fluorine on Aliphatic Carbon
Atoms**

SPECIFICATION NO. 955,898

The inventors of this invention in the sense of being the actual devisers thereof within the meaning of Section 16 of the Patents Act, 1949 are Erich Klauke, Am Telegraf 45 b, Leverkusen, Germany; Herbert Schwarz, Florastrasse 12, Opladen Germany; Hans Holtschmidt, An der Ruthen 2, Köln-Stammheim, Germany, all of German nationality.

THE PATENT OFFICE

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atoms, the chlorine atoms can be simply replaced by fluorine by reaction with anhydrous hydrofluoric acid.

- 20 Isocyanates which contain aliphatically combined fluorine atoms are known *per se* and they are prepared by the conventional processes from the corresponding amines by phosgenation or from the carboxylic acids by a Curtius degradation (Ann. 562, 75 (1949); J. chem. Soc. 1956, 3428).

- 25 According to prior knowledge concerning the exchange of chlorine for fluorine in anhydrous hydrofluoric acid, it was not to be anticipated that chlorinated isocyanates can be transformed by the process of the invention into fluorinated isocyanates. Thus, it is known that most nuclear substituents interfere with the exchange of chlorine in benzo-trichloride (Ang. Chem. 52,458 (1939)).
- 30 Apart from chlorine, only the phthalimide grouping permits a sufficient fluorination. By way of example, trichloromethyl benzonitrile cannot be further fluorinated with hydrofluoric acid.

- 40 It must be all the more surprising that with the present process, under extraordinarily gentle conditions, the chlorine exchange takes

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hydrofluoric acid on benzal chloride. On the other hand, the present invention shows that benzal chloride isocyanates can be fluorinated with hydrofluoric acid.

Fluorination in the aliphatic series, with the exception of methyl chloroform, cannot be conducted without catalysts, and the latter only at temperatures of 150° C. (Ang. Chem. 52,459 (1939)).

However, it was also not to be readily expected that the isocyanate group which is very reactive in the aromatic series does not initiate any, or only slight, secondary reactions under the conditions of the present process. Anhydrous hydrofluoric acid is a known Friedel-Crafts-catalyst and it is known that the isocyanate group condenses under the action thereof to acid amides.

It is certainly stated in German Specification 1,092,462 that aromatic isocyanates can be alkylated in anhydrous hydrofluoric acid, but it could be justifiably assumed that a special case is involved here. From the chemistry concerning anhydrous hydrofluoric acid, it is known that it is just under alkylation conditions that some compounds behave quite differently than otherwise in hydrofluoric acid (Ang. Chem. 56,341 (1943)). For

example, chlorinated hydrocarbons such as butyl chloride or amyl chloride in anhydrous hydrofluoric acid change into chloro-alkanes with longer and shorter chain lengths, whereas they do not show any such reactions in the same medium under alkylation conditions. Similarly different behaviours are also shown by alcohols and olefines.

Suitable isocyanates which are chlorine-substituted on aliphatic carbon atoms can for example be prepared according to German Patent 947,740 and British specification No. 916275. To be mentioned in detail are α,α -dichlorobenzyl isocyanate, 1,1,2,2-tetrachloroethyl isocyanate-1, *o*-, *m*-, *p*-trichloromethylphenyl isocyanate, α,α -dichlorinated *n*-propylphenyl isocyanates, α,α -dichlorinated ethylphenyl isocyanates, 1,1,2,2-tetrachloroethyl-*o*-phenyl isocyanate, bis(4-isocyanatophenyl) dichloromethane, trichloromethylphenylene-2,4-diisocyanate, 2-trichloromethyl-6-chlorophenyl isocyanate, 2-dichloromethyl-4-trichloromethylphenyl isocyanate. Trichloromethyl groups such as those present in trichloromethylphenyl isocyanate, can be changed particularly smoothly into the corresponding trifluoromethyl group.

The replacement of the chlorine atoms by fluorine takes place in stages. The intermediate stages can frequently be isolated, depending on the reactivity of the trichloromethyl group and by maintaining certain conditions as regards time and temperature.

When carrying out the reaction, the hydrofluoric acid is used both as a reactant and as a solvent. Consequently it will always be advantageous to use it in excess. Naturally, the hydrofluoric acid, in its capacity as a solvent, can also be replaced or supplemented by inert organic solvents, such as diethyl ether, tetrahydrofuran, dioxane, nitrobenzene. Occasionally, it is also advantageous to add those organic solvents in which the hydrofluoric acid is only partially soluble and the forming hydrochloric acid is not soluble, such as benzene, toluene, chlorobenzene.

The reaction temperature is advantageously between -20°C . and $+20^{\circ}\text{C}$. The reaction is usually started at low temperatures, advantageously from -5°C . to 0°C ., and it is raised to 20°C . and higher, depending on the strength of the evolution of hydrogen chloride. The reaction can also be carried out at higher temperature in pressure vessels.

Analysis: $\text{C}_8\text{H}_5\text{ONF}_3$
 calculated: C=51.4% H=2.14% N=7.48%
 found: C=51.58% H=2.28% N=7.49%

134 g. of *p*-difluorochloromethylphenyl isocyanate (=33% of the theoretical).
 yellowish liquid with a $\text{bp}_{10}=83-84^{\circ}\text{C}$;
 $n_D^{20}=1.5100$

Analysis: $\text{C}_8\text{H}_5\text{ONF}_2\text{Cl}$
 calculated: F=18.7%
 found: F=19.1%

The reaction mixture can for example be worked-up by distilling off the hydrofluoric acid and blowing off the reaction product at elevated temperature with nitrogen or carbon dioxide. For splitting the primarily formed carbamic acid fluoride into isocyanate and hydrofluoric acid, the blowing-out operation is preferably carried out at high temperature, followed by distillation.

Since some of the carbamic acid fluorides are considerably more stable than the corresponding carbamic acid chlorides, it is sometimes possible to isolate the isocyanates in the form of the carbamic acid fluorides by distillation.

The products of the process serve as initial products for dyestuffs, pest-control agents and pharmaceutical compounds.

In order that the invention may be more clearly understood the following Examples are given by way of illustration only:—

EXAMPLE 1.

200 cc. of anhydrous hydrofluoric acid are run into 473 g. (2 mol) of *p*-trichloromethylphenyl isocyanate over a period of $1\frac{1}{2}$ hours. The temperature in the reaction vessel is kept between 18 and 20°C . during this period. During the addition, there is vigorous evolution of hydrogen chloride. Stirring is continued for 1 hour at the same temperature, the evolution of hydrogen chloride practically ceasing towards the end.

The excess hydrofluoric acid is distilled off *in vacuo*. After adding 100 cc. of xylene the substance is heated to an internal temperature of about 135°C . for decomposing the carbamic acid fluoride, a weak stream of CO_2 being constantly conducted through the reaction mixture. After adding 3 to 5 g. of active carbon, the solution is allowed to cool while stirring, whereupon it is filtered and the filtrate is distilled immediately. The first distillation serves only to separate the reaction products from unreacted initial material and small quantities of resinification product. From the crude distillate, it is possible to isolate the following compounds by fractional distillation under reduced pressure:

132 g. of *p*-trifluoromethylphenyl isocyanate (=35% of the theoretical).

Colourless liquid with a $\text{bp}_{10}=58-59^{\circ}\text{C}$;
 $n_D^{20}=1.4713$.

NCO-value, found 22.3% (calculated 22.5%)

EXAMPLE 2.

508 g. (2.5 mol) of *o*-isocyanato-benzal chloride are initially provided and cooled to a temperature of -5°C . 250 cc. of anhydrous hydrofluoric acid are introduced dropwise over a period of 20 minutes. In spite of thorough cooling with brine, the

temperature rises to +15° C. On completing the addition, the temperature is +4° C. The reaction mixture is slowly heated to 20° C., so that a steady evolution of hydrogen chloride is maintained. At this temperature, stirring is continued for another 2 hours and then the reaction is stopped in order to avoid secondary reactions which lead to resin formation, although the evolution of hydrogen chloride is still not terminated.

100 cc. of chlorobenzene are added and the mixture is initially heated slowly in order to distil off the excess hydrofluoric acid. From 40° C., a gentle stream of CO₂ is conducted through the reaction mixture, which is heated to an internal temperature of 120° C. until the added chlorobenzene starts to distil off.

With the subsequent distillation, 295 g. of distillate are obtained in addition to 174 g. of unmodified initial material, the said distillate containing the following fluorine-containing reaction products in the pure fractions:

1. o-difluoromethylphenyl isocyanate
bp₁₃=84–86°, n_D²⁰=1.5049

Analysis: C₈H₆ClF₂NO

calculated: C=39.74% H=1.65% Cl=14.7% F=31.54% N=5.8%

found: C=39.8% H=1.77% Cl=15.0% F=31.38% N=5.9%

EXAMPLE 4.

350 cc. of anhydrous hydrofluoric acid are placed in the reaction vessel and cooled to –4°. 354 g. of 2,4-bis-(trichloromethyl)-phenyl isocyanate (bp_{0.5}: 147–150°; n_D²⁰: 1.6050) are run in while stirring well within 15 minutes. After completing the addition, the temperature has risen to +4°. By cooling, the temperature is kept during the fairly vigorous reaction between 5 and 10° C. After 2 hours, the temperature is raised over a period of another 3 hours to 19° C. and stirring is continued at this temperature for 12 hours. 200 cc. of chlorobenzene are now added, the excess hydrofluoric acid is extracted *in vacuo* and the substance is heated to 130° C. while passing through a weak stream of CO₂. After adding 3 g. of active carbon, the substance is cooled, filtered and the filtrate is distilled.

Distillation yields:

124 g. of 2,4-bis-(trifluoromethyl)-phenyl carbamic acid fluoride (=45% of the theoretical). Bp₁₃: 73–74° C.; n_D²⁰: 1.4325

analysis: C₈H₄F₆NO

F: calculated 48.3% F: found 47.8%

EXAMPLE 5.

By chlorination of toluylene-2,4-diisocyan-

Analysis: C₈H₃N₂O₂F₄Cl

calculated: C=38.15 H=1.06 N=9.9 Cl=12.57 F=26.9

found: C=38.12 H=1.13 N=9.92 Cl=12.70 F=26.2

In addition, another 197 g. of a liquid are isolated, this consisting predominantly of unmodified starting material.

analysis: C₈H₃F₂NO

calculated: F=22.45%

found: F=22.54%

2. o-fluorochloromethylphenyl isocyanate

bp₁₃=103–105°, n_D²⁰=1.5410;

analysis: C₈H₆ClFNO

calculated: F=10.25%

found: F=10.10%

EXAMPLE 3.

240 g. of anhydrous hydrofluoric acid are added to 234 g. of 2-trichloromethyl-4-chlorophenyl isocyanate in 100 g. of chlorobenzene at 0° C. over a period of 30 minutes, the temperature is allowed to rise in 1 hour to 10° C. and then the mixture is heated for another hour to 20° C. At this temperature, the mixture is stirred for another 3 hours. Thereafter, the excess hydrofluoric acid is distilled off *in vacuo*, the substance is heated while introducing CO₂ to 100° C. and the residue is distilled from glass under reduced pressure. There are obtained 174 g. (=74% of the theoretical) of 2-trifluoromethyl-4-chlorophenyl-carbamic acid fluoride of the bp₁₄=92–93°; mp: 38°.

ate, both in the side chain and in the nucleus, the 2-trichloromethyl-4-chlorobenzene-1,5-diisocyanate (bp_{0.4}: 154–158° C.; n_D²⁰: 1.6309), is obtained as starting material for the fluorination reaction.

1 litre of anhydrous hydrofluoric acid is initially supplied and cooled to –2° C. Then 1 kg. of 2-trichloromethyl-4-chlorobenzene-1,5-diisocyanate is added over a period of 40 minutes. The temperature thereby rises to +3° C. in spite of cooling. The initially only moderate evolution of HCl becomes rather violent after about 20 minutes. During this vigorous evolution of gas, the temperature is kept between –5° and 0° C. After approximately 4 hours, the temperature is raised in proportion as the evolution of HCl subsides. After a total running time of 24 hours, the mixture is worked up in the usual manner and there are obtained 486 g. of the mono-carbamyl fluoride derived from 2-trifluoromethyl-4-chlorobenzene-1,5-diisocyanate. bp₁: 93–96° C.; mp 68° (from benzene).

This corresponds to a yield of 54% of the theoretical, based on the product used, or 67% of the theoretical, based on reacted product.

EXAMPLE 6.

400 cc. of anhydrous hydrofluoric acid are placed in the fluorination apparatus. At an

internal temperature of +10°, 400 g. of 1,3-bis - (trichloromethyl) - benzene - 4,6 - diisocyanate are run in over a period of 3 hours. There is copious evolution of HCl, and this subsides somewhat after another 2 hours. The temperature is now slowly raised to 19° C. and the mixture is stirred for another 15 hours.

After working up, there are obtained: 200 g. (59% of the theoretical) of 1,3-bis - (trifluoromethyl) - benzene - 4,6 - bis - carbamyl fluoride with a melting point of 102.5° C. (from light benzine)

Analysis: $C_{10}H_4N_2O_2F_4$
 Calculated: C=35.74 H=1.19 N=8.33 F=45.27
 found: C=36.08 H=1.30 N=8.33 F=45.17

Molecular weight 336.12

EXAMPLE 7.
 With a rise in temperature from 6—18° C., 300 g. of tetrachloroethyl isocyanate (n_D^{20} : 1.5080) are added in 50 minutes to 200° C. of anhydrous hydrofluoric acid. The initially copious evolution of HCl subsides after 4 to 5 hours to about half. Stirring is continued for 15 hours at 15° C. and the excess hydrofluoric acid is distilled off. The residue of 228 g. contains as main fraction an isocyanate which distils over from 100 to 110° under normal pressure and has a refractive index of n_D^{20} : 1.4160. The fluorine content is 17.6%.

stituted with fluorine on aliphatic carbon atoms, which comprises reacting anhydrous hydrofluoric acid with an isocyanate which has chlorine substituents on aliphatic carbon atoms.

2. A process as claimed in claim 1, substantially as described with reference to any one of the Examples.

3. Carbamic acid fluorides and isocyanates, when prepared by the process claimed in either of the preceding claims.

WHAT WE CLAIM IS:—

1. A process for the production of carbamic acid fluorides or isocyanates which are sub-

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